

### **REMARKS**

Applicant offers the following remarks in support of the patentability of the claimed invention.

### **Objections and Concerns Under Section 112**

Claims 3 and 13 are cancelled without prejudice, thus rendering moot the previous objections and rejections under Section 112.

### **The Claimed Invention Is Nonobvious Over The Cited Combination of References**

The only independent claim pending in this application is claim 1. All other pending claims are dependent from claim 1 or from an intervening claim. The Examiner had previously cited Hajukiewicz et al. (WO 00/03022) in view of Goodman et al. (US 5,629,175) as rendering claim 1 obvious and unpatentable under 35 USC §103(a). The instant Office action adds Daniell (WO 99/10513) as a third reference cited in combination with Hajukiewicz et al. and Goodman et al. in a rejection of claim 1 under Section 103.

The Examiner has also noted on page 5 of the instant action that "Applicant's arguments focused only the rejection of Hajukiewicz et al. (WO 00/03022) in view of Goodman et al. and did not address the rejection of claims 9-13 over Hajukiewicz et al in view of Goodman et al and further in view of Daniell."

Applicant acknowledges the Examiner's comment. However, as the Examiner knows, if an independent claim is found patentable, its dependent claims will be

automatically deemed patentable as well, since they do nothing more than add features to the invention recited in the independent claim. Accordingly, while the Examiner is required by Office policy to address each claim, it is quite customary, even recommended standard practice, for counsel to focus his/her arguments on the independent claims alone and to remain silent with respect to dependent claims. Again, the reason being that if the overlying independent claim is shown to be patentable, the respective dependent claims will necessarily also be patentable. Applicant offers these comments by way of explanation as to why these remarks focus only on claim 1.

With regard to the obviousness rejection of claim 1, the Examiner has previously noted that that Hajukiewicz et al. teach transformation of tobacco chloroplasts but do not teach expression of insulin-like growth factor (IGF) in tobacco plastids. The Examiner has also recognized that Goodman et al. teach expression of mammalian proteins, including insulin-like growth factor, in plants. Goodman et al., however, only describe nuclear transformation of plants, not plastid transformation. Therefore, the Goodman et al. reference teaches nothing about chloroplast transformation.

The obviousness rejection of claim 1 is now reasserted with the addition of the reference by Daniell, which is cited by the Examiner to "teach a plastid expression vector that can be used to transform the chloroplasts of a wide variety of plant species." The Examiner further contends that "it would have been obvious to one of ordinary skill in the art to modify the method of expressing a mammalian protein in tobacco plastids as taught by Hajukiewicz et al to use the insulin-like growth factor as the mammalian protein, as described in Goodman et al." The Examiner also contends that "one of

ordinary skill in the art would have been motivated to do so because substitution of one desirable and economically important mammalian protein for another is an obvious design choice."

Applicant has previously argued that the Goodman et al. reference does not teach plastid transformation and that the reference by Hajukiewicz et al. does not even discuss spacer regions. The reference by Goodman et al., as pointed out by the Examiner, mentions insulin-like growth factor, however, the other two cited references make no mention of IGF. The newly added Daniell reference teaches a universal vector useful for transforming the chloroplast genome but this reference also does not mention insulin-like growth hormone (an electronic search of the document failed to find any use of the term). The Examiner, however, contends that one of ordinary skill in the art would have been able to combine these three references to achieve the invention recited in claim 1, the claimed invention being, therefore, obvious and unpatentable.

Applicant respectfully disagrees and provides the following scientific, not legal, arguments and requests that the Examiner take official notice of these facts. Cognizant that "attorney argument" is not given the weight of evidence by the Office, counsel nevertheless points out that the following are facts accepted by the scientific community and not legal arguments, thus the request that the Examiner, who is a trained scientist, take official notice thereof.

It is accepted scientific fact that successful production of proteins in chloroplasts depends on two types of factors: chloroplast-specific factors and gene-specific factors. More specifically, production of proteins can be divided into five necessary steps: integration, transcription, translation, stabilization, and function. The first three steps

(integration, transcription, and translation) fall into the chloroplast-specific factor category and may be considered somewhat predictable. The latter two steps, however (stabilization and function), are gene-specific factors and are quite unpredictable.

Stabilization and functionality of the protein are unpredictable because they are gene-dependent and are, in fact, dependent on the intrinsic properties of the specific polypeptide being produced by plastid transformation. First, stabilization depends on the amino acid sequence of the protein's polypeptide and whether the sequence contains protease cleavage sites. Proteases in chloroplasts have not been fully characterized, so that it is unpredictable whether a particular polypeptide produced in the chloroplast will or will not be hydrolysed by proteases. Stabilization and function also are known to depend on the secondary and the tertiary structure of the protein, which in turn are affected by the amino acid sequence of the polypeptide. If a polypeptide can fold into its secondary and then tertiary conformations quickly, then the protein will be resistant to proteases and will be more stable. Further, a protein that is able to assume its secondary and tertiary structure is also more likely to be functional.

So, in summary some aspects of protein expression in chloroplasts, such as stabilization and function, are unpredictable because they are intrinsic to the polypeptide sequence being expressed. Consequently, there is no *a priori* expectation of success in achieving production of an active foreign protein by chloroplast transformation. For those reasons, the claimed invention should not be considered to have been obvious to those of ordinary skill in the art at the time the present application was filed.

In re Patent Application of  
Daniell  
Serial No.: 10/519,820  
Filed: 12/30/2004

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Accordingly, Applicant respectfully requests that the claim rejections under Section 103(a) be withdrawn and that the application be allowed.

**Conclusion**

If the further processing of the application could be facilitated through a telephone conference between the Examiner and the undersigned, the Examiner is invited to contact undersigned counsel.

Respectfully submitted,

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